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TO: Examiner Bruce Campell COMPANY NAME: USPTO, Patent Group 1632

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Re: Reply Brief mailed 4/5/99 via Express mail
USSN 08/410,539
Filed 3/24/99
TRANSGENIC UNGULATE COMPOSITIONS AND METHODS

Dear Examiner Campell:

Please find attached 2 additional copies of the Reply Brief mailed yesterday, 4/5/99.

If you have any questions, do not hesitate to call me at (312) 214-8316.

Very truly yours,
Alice O. Martin

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellant:	Matthew B. Wheeler	:	
Serial No.:	08/410,539	:	
Filed:	March 24, 1995	:	Group Art Unit: 1889
For:	TRANSGENIC UNGULATE COMPOSITIONS AND METHODS	:	Examiner: Bruce Campell

Alice O. Martin for Appellant

REPLY BRIEF TO EXAMINER'S ANSWER

This paper is filed in response to the Examiner's Answer mailed February 5, 1999.

The Status of the Claims Appears to be Correct

Appellant does not understand the examiner's statement that

> ...the status of the claims contained in the brief is incorrect.

Examiner's Answer, page 2

Because the examiner's statement of the claims

> ...1-6, 9-12 and 15-20

is the same as stated by appellant, that is,

> Claims 1-6, 9-12 and 15-20 are the object of this Appeal.

Main Brief on Appeal, page 1

These are also the claims listed in the Appendix of the Main Brief on Appeal.

The minor error in claim 1 pointed out by the examiner in the Appendix of appellant's Main Brief on Appeal is noted.

A Summary of the Examiner's Answers

The only remaining rejection is of claims 1-6, 9-12 and 15-20 under 35 U.S.C. § 112, ¶1, on the basis that the specification does not enable one skilled in the art to use the invention, commensurate with the claims, with any ungulate other than swine. This rejection is appropriate where the written description fails to enable a person skilled in the art to make and use the invention as broadly as it is claimed without undue experimentation at the time the patent application is filed.[1] The examiner depended on various references cited by the appellant to establish skepticism as to the appellant's ability to claim a broad genus without demonstrating specific working examples for each species. The examiner argued that:

1. more that one example is needed in to claim an entire genus, particularly in an unpredictable art;

2. because differences exist within ungulate species, appellant needs more working examples to demonstrate the enablement of his invention beyond merely swine;

3. appellant's production of ES-cells in sheep does not establish a persuasive example because those cells were not demonstrated to contribute to the germ line; and

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[1] The enablement standard is set forth at Section 112, ¶1, which recites:
"The specification shall contain a written description of the invention and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention." 35 U.S.C. § 112, ¶1.

4. there is no evidence that the methods described in the specification produce embryonic stem cells (ES-cells) of species other than swine.

REPLY

The Specification is Enabled for a Method to Produce Ungulates

In response to the examiner'argumentsts summarized above, appellant argues as follows:

1. **There is no statutory requirement to provide more than one example; in fact, *no examples are required***

The examiner's conclusion that

> It is well settled that more than one working example **may** be required to enable a broad genus, particularly in an unpredictable art. *Citing* MPEP 2164.02

Examiner's Answer, page 4,

correctly acknowledges that one working example may suffice for enablement, but fails to take into account that **none are required** by law.

The examiner relies on the MPEP for support for his position, but further consideration of the MPEP reveals that there is no requirement for even one, much less more than one, "working examples".

> Compliance with the enablement requirement of 35 U.S.C. 112, ¶1, **does not turn on whether an example is disclosed.**

MPEP 2164.02, *emphasis provided.*

Appellant's claims should not be limited to swine just because he has shown use of swine in the method is operational.

> All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims see, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).
>
> As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. *In re Moore*, 439 F.2d 1232, 1236, 169 USPQ 236, 239 (CCPA 1971).

MPEP 2164.08

> ...lack of working examples or lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement.

MPEP 2164.02

> Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation.

MPEP 2164.02

> ...even in unpredictable arts, a disclosure of every operable species is not required.

MPEP 2164.03

2. **More working examples are not needed**

Lack of a working example should not be the sole reason for a rejection. Only an enabling disclosure is required for patentability, not a disclosure comprising all actual embodiments.

> The test for working examples and a claimed genus is *representative samples* together with a *statement applicable to the genus* as whole,

> provided *one skilled in the art would expect the claimed genus* to be used *without undue experimentation.*

35 U.S.C. § 112, 1; MPEP § 2164.02 (*emphasis added*).

In reply to the comment regarding *Wands*, in the Examiner's Answer, page 7, appellant is well aware that relevant factors that establish whether experimentation, if any, is undue, includes, among other things, the presence or absence of working examples, and the predictability or unpredictability of the art. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). But in *Wands*, referring to what is meant by "undue", the court stated that

> Time and difficulty of experiments are not determinative if they are merely routine.

The examiner provides no argument that routine experimentation would not suffice. The examiner admits there is enabling disclosure for swine and, as MPEP § 2164.02 states

> But because only an enabling disclosure is required, applicant need not describe all actual embodiments.

3. Germ line transmission is not required for chimeric ungulates

When appellant questioned what a "working example" meant in the present case, appellant did so not because appellant was unaware of the *Wands* factors, but because appellant questioned on what legal basis the examiner decided that more than one working example was required and why the example provided for sheep was defective for purposes of enablement because it did not show germ line transmission. As discussed in the application, germ line transmission is required to produce transgenic animals, by definition. However, no scientific or legal basis exists to require

this for chimeric animals, because these are by definition, mixtures of genetically different cells, not necessarily in the germ line. It is, of course, preferred to have germ line chimeras to produce transgenic animals, but the claimed methods are not to transgenic animals.

4. **It is not correct that there was "no evidence" that the methods provide ES cells of species other than swine**

The examiner stated that

> Appellant argues that the specification provides guidance regarding species other than swine. This may be true, but there is no evidence that the methods described in the specification produce ES cells of species other than swine.

Examiner's Answer, page 7.

> In *In re Goffe*, 542 F.2d 564, 567, 191 USPQ 429 (CCPA 1976), the court stated:
>
> > [T]o provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for "preferred" materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts.

MPEP 2164.08

It appears as if the examiner is really questioning not enablement of ungulates, but whether the enabled invention would be operative in species other than swine within ungulates. Appellant is not required to prove operability in all

species to claim a genus. In fact, the examiner acknowledges the operability of the working example in swine and only criticizes the working example in sheep because

> The specification does not provide any working examples or specific guidance regarding production of embryonic stem (ES) cells of species other than swine.

Examiner's Answer, page 5.

> The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabling. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make disclosure nonenabling).

MPEP 2164.08(b)

As the Court of Appeals for the Federal Circuit recently stated:

> NRT is indeed correct that a claim is not invalid for lack of operability simply because the invention does not work perfectly under all conditions. See *Hildreth v. Mastoras*, 257 U.S. 27, 34,66 L.Ed. 112, 42 S. Ct. 20 (1921) ("The machine patented may be imperfect in its operation; but if it embodies the general principle and works... it is enough"); *Decca, Ltd. v. United States*, 210 Ct. [**18] Cl. 546, 544 F.2d 1070, 191 USPQ (BNA) 439 (Ct. Cl. 1976) ("The mere fact that the system has some drawbacks, or that under certain postulated conditions it may not work... does not detract from the operability of the disclosed equipment to perform its described function.")

National Recovery Technologies, Inc. v. Magnetic Separation Systems, Inc. and Garry R. Kenny, 166 F.3d 1190 U.S. App. LEXIS 1671; 49 USPQ.2D (BNA) 1671.

The existence of inoperative embodiments does not destroy patentability. Moreover, if the method does not work in a particular species, no one will want to infringe the claim or pay the Appellant royalties, so the existence of a patent on all ungulates would not be helpful to the patentee. On the other hand, if an infringer practices all steps of the method and escapes infringement just because the infringer produced a chimeric sheep instead of a chimeric swine, that would be unfair to the patentee who was the first to develop the method.[2]

No Argument is Presented by the Examiner that the *Method* is Not Enabled

Moreover, the claims on appeal are all **method** claims. The examiner provides **no argument that the steps in the method claim are not enabled.** The examiner only rejects the claims **because the method might not work in all ungulates.** This is not the "clear and convincing evidence" required for an enablement rejection.

> In *United States v. Telectronics Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989), the court reversed the findings of the district court **for lack of clear and convincing proof that undue experimentation was needed.** The court ruled that since one embodiment (stainless steel electrodes) and the method to determine dose/response was set forth in the specification, the specification was enabling.

MPEP 2164.06(a), *emphasis provided.*

Whether or not the invention is operative in all ungulates is irrelevant to patentability of the method, as discussed herein.

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[2] The Doctrine of Equivalents cannot be relied on to include other ungulates if the prosecution history limits claims to swine.

The examiner cited to publications that predated the invention, therefore contained skepticism that any ungulate ES cells could be produced. But Appellant has disclosed, as the examiner agrees, success in producing ES cells in swine using the claimed method. This would be likely to replace any skepticism for swine, and has not been replaced by skepticism about other ungulates after learning of the claimed method. That differences among ungulates, e.g., in embryonic development, are reported (Examiner's Answer, page 5) will only facilitate application of the present invention to all ungulates. Extrapolation will be easier from swine based on these reports, e.g., regarding timing of embryonic stages..

The examiner has not provided any arguments to show that persons skilled in the art could not perform each step of the claimed method in any species. For example, for claim 15, those of skill in the art know how to dissociate cells (also disclosed in the specification), and have the formulas for conditioned stem cell medium disclosed in the specification. Also disclosed are the "morphological features and growth parameters characteristic of an embryonic stem cell culture".

Persons skilled in the art would most likely try the method on an ungulate of interest to them -- for example, a farm animal or an animal known to be useful for medical research, transplantation and the like. Persons of skill would hardly rush out to try the method on all ungulates, including the exotic species the examiner lists from a dictionary definition of "ungulate". Persons of skill following the guidance in the specification would expect to work on those ungulates closest to swine (and sheep) in characteristic that relate to the steps in the claims.

There is no evidence that the method of the invention would require undue experimentation to practice it on species other than swine. As the examiner notes, sheep ES cells fitting the criteria of claim 15 have been produced in addition to swine ES cells.

Conclusion

The examiner errs in rejecting claims 1-6, 9-12 and 15-20 under 35 U.S.C. § 112, ¶1 because he maintains that two ungulate genera examples - swine and sheep are insufficient to support claims to all ungulates. He also questions whether the invention would be operative for sheep.

There is no legal basis to require any working example, much less more than the two represented in the pending application. Also, even if the inventions were inoperable for sheep, this would not destroy patentability. Moreover, the method is enabled because no argument is presented that any steps in the method claims are not enabled.

Accordingly, the Board is requested to REVERSE the Final Rejection of January 9, 1998.

Respectfully submitted,

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April 5, 1999